



**NCI-FREDERICK
INSTITUTIONAL BIOSAFETY COMMITTEE**

Minutes – February 21, 2006
NCI-Frederick

The NCI-Frederick Institutional Biosafety Committee was convened at 12:02 p.m. in the Building 549 Executive Board Room with the following members in attendance:

Dr. Randall Morin, Chair
Dr. Henry Hearn
Mr. Lucien Winegar
Dr. Michael Baseler
Dr. Bruce Crise
Dr. Dan McVicar

Ms. Alberta Peugeot
Ms. Theresa Duley, Secretary
Dr. David Garfinkel
Dr. Stephen Hughes
Dr. Paul Nisson

Members not in attendance: Dr. Melinda Hollingshead, Dr. Stephen Creekmore, and Dr. Jeanne Herring

Others in attendance: Ms. Cara Leitch, Dr. Scott Keimig, Dr. Kimberlee Wallace, Dr. Phil Gomez, Mr. John Madsen, and Ms. Barbara Brooks

INTRODUCTION

Dr. Morin called the meeting to order.

Dr. Morin requested the IBC members to review the January 2006 meeting minutes distributed at today's meeting. A vote will be obtained by through email on March 3 for final approval of the January 2006 minutes.

PROTOCOL REVIEWS

NEW BUSINESS

06-15 (Dr. Tarr):

The following questions were brought to the attention of the IBC regarding this IBC submission.

- 1) How much plasmid is being handled?
- 2) Is the method of decontamination effective against plasmids and DNA? Keep the thought in mind that although plasmids are not purposely mixed together, if the decon for eliminating plasmids is not effective, then when work is initiated with another plasmid, the potential for mixing plasmids may occur.
- 3) Can HIV be reconstituted if coding regions are put together? Why or why not?
- 4) Please provide the QA information sheets documenting what the plasmids are supposedly comprised of. Do the plasmids cover all of the HIV genome?
- 5) What personal protective equipment will be provided for the individual performing filling operations? Are aerosol hazards addressed? Surgical masks may not be sufficient and the committee encourages VPP to look into the use of PAPR's or N100 respiratory protection, which may require fit testing, medical surveillance and/or an annual training.
- 6) Is there a validation test in place to ensure that the plasmid is removed or inactivated?
- 7) How do you minimize the risk of vials (glass) breaking during transport, and if a spill were to occur, would packaging be appropriate to contain liquid spill and to prevent mixing of individual packages. Provide leak-proof transport and use holding devices for vials.
- 8) Will you perform a riboflavin test run with PCR to detect plasmid scattering? Although the adenovirus being used is not intended to be replication competent, it could possibly be contaminated given the large volumes of adenovirus with HIV in it.
- 9) Please verify that 180 grams of DNA will be filled and there will be approximately 10^{15} adenovirus particles.
- 10) Confirm all filling operations will be performed in a barrier isolator (class 100) and further define what this consists of. Elaborate on the lack of aerosol exchange.
- 11) Clarify shipping procedures and packaging operations.
- 12) Please clearly identify which portions are missing from the genome.
- 13) Clarify the volumes of adenovirus to be used.
- 14) Will a VHP decontamination be done between each independent run or study?
- 15) Is VHP effective in killing plasmids? Is there data to validate this? A direct assay, such as PCR, would be effective in determining efficacy of VHP in inactivating plasmids.
- 16) Clarify if a sporicide will also be used, if so what type, and how efficacious it is. Will potassium hydroxide or Spor Klenz, peroxide, or peracetic acid be used?
- 17) The rate of filling is to be determined—40 vials per minutes--is this known yet? Filling at a slower rate will minimize potential for aerosol generation.
- 18) Employees may not be permitted to work in the lab if they are ill or have compromising health concerns (respiratory infections or open wounds).
- 19) Clarify manual filling will be performed in a BSC.
- 20) Automatic filling procedures are completely enclosed so worker contact with infectious material is not possible—is this true immediately before or after beginning filling operations-during set-up and take down operations?

21) If there were a spill of 5L or more, would a standard BSC be able to contain the spill within the cabinet?

22) An EHS site safety assessment will be completed prior to initiation of work to view set up operations, riboflavin run, and dismantlement of operations post-fill.

23) Ensure the paperwork reflects the implementation of a macerator system, followed by steam sterilization and final disposal.

The IBC members granted a conditional approval for the VPP to receive and store DNA, with the request that the material not be distributed within or used until applicable registrations documents are received and approved through EHS.

Dr. Crise made a motion to defer approval on this registration proposal until the above items have been sufficiently addressed. Dr. Hughes seconded and all were in favor.

06-08 (Dr. Hou):

This proposal only involved recombinant material and no virus. Dr. Crise recommended to approve the registration as submitted, Dr. Morin seconded and all were in favor.

06-12 (Dr. Moschel):

1) Please provide a cell line description

2) Define the compounds of interest

3) Define your sonification procedures since this is a relatively high hazard procedure.

4) A3: Please provide a more detailed explanation.

5) A4: We need you to submit an SOP describing all procedures and practices and please clarify what is meant by "laminar flow cabinet".

6) EHS will need to perform a lab inspection of your area prior to initiation of work.

7) Please further describe the training programs implemented within the lab for employees to address hazards and mitigation measures, and to ensure employees are well versed in laboratory practices and procedures.

Dr. Crise made a motion to defer approval pending sufficient responses to the items above, Dr. Baseler seconded and all were in favor.

06-16 (Dr. Acharya):

1) Please clarify how you will transport samples.

2) Question B4 – N/A is not an appropriate answer, explain rDNA role in experiments.

3) Question B5-Further define the nature of the exon trap(is it a viral gene trap?).

4) Question B2b-Clarify what is being done with yeast.

- 5) For questions A3-A5, please integrate answers from SOP into registration document. Describe potential risks.
- 6) Question B9a, specify antibiotic resistance, and reference response in B6a above.
- 7) Address in B6a if there are any human hazards associated with yeast or 3T3 cells.
- 8) Addendum 1 needs signatures.

Dr. Crise made a motion to recommend conditional approval pending resolution of the above items, Dr. Garfinkel seconded and all were in favor.

06-20 and 06-21 (Dr. Crise):

Please clarify that there will be no cultures brewing at the same time.

- 2) Please state that employees will not work on different infectious materials on the same day.
- 3) Steve had asked about vector origin and validation to ensure compatibility and quality control measures are in place.
Specifically state how adenovirus and HIV are separate (we realize this is already stated in your HIV doc but were unsure if this should be stated again in the adeno doc).
- 2) If 433 is the development lab, will this be the only place where lentivirus work occurs?
- 3) Separate virus from plasmids (already in HIV doc)
- 4) Different incubators (completed in HIV doc)
- 5) Explain how each infectious material will be kept separate?
- 6) Don't work on different things on same day.
- 7) Risk category clear to employees and they are informed (this is done with tables and risk doc)
- 8) Ensure no HIV envelope (done in HIV doc)
- 9) Vector origin and validation - quality control to ensure compatibility.

Dr. Hughes made a motion to recommend approval pending the line items above being addressed, Dr. Baseler seconded and all were in favor.

06-18 (Dr. Malyguine):

Please clearly state that your group will only be working with the blood from NHP's and not the NHP's themselves. Please state the source of these cells and how they will be transported/received.

- 2) Be aware and inform employees involved in this work of risks associated with adenovirus (for cases such as pregnancy or for when employees may bring adenoviruses into the work environment in the form of a cold, etc) - I would refer you to Health Canada MSDS or EHS safety grams for starters. Is adeno new to this lab?
- 3) B6C-We believe this response needs some additional information or that this response is not correct-please explain further. Infectious? Non-replicative?

Please further demonstrate that the material you are receiving is in fact what you expect to receive (to ensure all hazards are addressed and for quality control purposes - verify source).

- 4) Are there any issues involving the NIH work coming here?
- 5) Is the vector potentially mobilizable?
- 6) Given that the group is working with macaque blood, are there any needs for additional medical surveillance for potentially exposed employees? Are there any unaddressed hazards inherent to rhesus macaque blood?
- 7) EHS will need to inspect the laboratory where this work will be performed prior to initiation of this work (please call me to set this up)
- 8) B5e and B5f: Is the virus attenuated? and B5F should be "YES"
- 9) Please further clarify the objective in what this research effort is trying to accomplish-what you intend to do with the results?
- 10) Safety would encourage you to talk with others about the hazards associated with working with adenoviruses, and how to best mitigate these hazards, to include implementing additional safe work practices, chemical disinfectants to be used rendered most effective against adeno, and other procedures that will help reduce the risk to employees

Dr. Morin made a motion to defer approval pending resolution of the above items, Dr. Baseler seconded and all were in favor.

RENEWALS

06-06 (Dr. Young):

All of the cell lines were sufficiently identified, additional information describing the retrovirus system was provided, and the safety risks associated with the retrovirus system were addressed.

Ms. Duley made a motion to approve, Dr. Crise seconded and all were in favor.

06-11 (Dr. Moschel):

- 1) Please provide a cell line description
- 2) Define the compounds of interest
- 3) Define your sonification procedures since this is a relatively high hazard procedure.
- 4) A3: Please provide a more detailed explanation.
- 5) A4: We need you to submit an SOP describing all procedures and practices and please clarify what is meant by "laminar flow cabinet".
- 6) EHS will need to perform a lab inspection of your area prior to initiation of work.
- 7) Please further describe the training programs implemented within the lab for employees to address hazards and mitigation measures, and to ensure employees are well versed in laboratory practices and procedures.

Dr. Crise made a motion to defer approval pending sufficient responses to the items above, Dr. Baseler seconded and all were in favor.

06-10 (Dr. Gorelick):

Three questions resulted from reviewing Dr. Gorelick's registration submission.

1) Will all work be conducted in a BSC? If not, please specify which laboratory procedures and operations will not be conducted inside the BSC.

2) Will you actually be culturing anything?

3) Will this work be conducted using standard BSL-2 practices, procedures and facilities?

Pending receipt of responses, and review by designated lead reviewers an email vote will be taken for final approval.

AMENDMENTS

04-10 (Dr. Wolff):

1) Please clarify further what murine viruses are being used? Is this standard MLV?

2) Are vector systems being used, are these vectorized viruses? If so, we need to know the specific vectors and their hazards.

3) There are concerns regarding the mixture of hazardous chemicals, KO animals, and vectors. If vectors are involved please address. Can you also speak to how the chemical hazards are addressed for employees with a potential for exposure.

4) Please verify where this work will be performed.

Dr. Hughes made a motion to approve pending resolution of the line items above, Dr. Crise seconded and all were in favor.

03-01 (Dr. Keller)

Keller (03-01) was conditionally approved by designated review (McVicar) based on adding the statement that the Id1 and Id2 knockouts were not made using viruses - they were made by transfection of a linearized targeting vector.

OUTSTANDING ITEMS

05-29 (Dr. Rane) – On hold.

05-52 (Dr. Xie) – Approval pending additional PI responses.

05-49 and Pathogen (Dr. Chatterjee) – On hold.

06-01 and 06-02 (Dr. Poon) - PI to address IBC questions.

05-60 (Dr. Kopp) - PI to provide additional information.

05-59 (D. Sohn/Perwez) - Animal facility manager to provide outstanding items.

OTHER BUSINESS

- 1) The IBC discussed the Student Intern Program and an impending meeting to discuss how to handle students obtained through the government systems who are working in laboratories under the direction and instruction of SAIC supervisors. The issue of minors working in laboratories and what materials they should be permitted to work with was also discussed.
- 2) Ms. Duley and Ms. Leitch called upon the committee for any comments regarding the draft updating the Policy and Procedure #604 to include all pathogenic material used at the NCI, to eliminate the restrictions of the document to only HIV. A final vote will be taken by email on March 3, 2006.

The meeting was adjourned at 2:43 p.m.

MINUTES RECORDED BY:

Theresa Duley, MPH
IBC Secretary
Biological Safety Officer, EHS

Cara Leitch
IBC Coordinator
Sr. Safety Specialist, EHS

APPROVED

Randall S. Morin, Dr. P.H.
Chairman, NCI-Frederick IBC
Director, EHS

DATE

xc: All Committee Members
Dr. Wiltrout
Dr. Reynolds

Mr. Eaton
Dr. Arthur
Mr. Bufter
Dr. Keimig